REMARKS/ARGUMENTS

Applicants respectfully request entry of this Amendment and reconsideration of this application.

By the amendments, Applicants do not acquiesce to the propriety of any of the Office's rejections and do not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997).

In the Claims

Claims 27-30, 32, and 41-46 are pending in this application. Claims 1-26, 31, and 33-40 have been previously canceled.

35 U.S.C. §102 Rejections

The rejection of claims 27-30, 41-43, and 44-46 under 35 USC §102(e) as being anticipated by Orme (7,288,261) has been maintained. Applicants respectfully traverse.

The Office states in the Office Action dated January 29, 2009 (hereinafter "OA") page 3,

> [h]owever, Applicants are respectfully directed to the summary section of Orme et al., specifically summary paragraph number 14, which sets forth that "Horwitz et al. 1995, claimed that Ag85 protein protected guinea pigs against aerosol TB. This study was said by the authors to demonstrate that immunization with the Mtb 30 kDa major secretory protein (Ag85A), alone or in combination with other abundant extracellular Mtb protein induced strong cell-mediated responses and substantial protective immunity against aerosol challenge with virulent Mtb bacilli in the highly susceptible guinea pig model of pulmonary tuberculosis."

Applicants do not see such a passage in the summary paragraph 14 of Orme. However, Orme column 3, lines 13-21 does recite the passage above. The first author of the study cited by Orme is the co-inventor of the instant application. The Applicants respectfully assert that the statements by Orme in this passage represent a typographical error or a misrepresentation. The Horwitz et al. paper (PNAS 92:1530-1534, 1995), attached hereto as Appendix A, does disclose the 30 kDa major

extracellular protein of *Mycobacteria tuberculosis*, however this protein is not the Ag85A protein. The 30 kDa protein corresponds to the Ag85B protein, also referred to as the product of the Rv1886c, or FbpB, gene (see Orme, Table 1). In the Horwitz et al. paper, of the *M. tuberculosis* proteins studied, only the 30 kDa protein was used alone; in addition, it was used in combination with other proteins. Hence, the protein referred to in the Orme passage above, where it was stated that the protein was used "alone or in combination with other abundant extracellular Mtb proteins" could only have been the 30 kDA Ag85B (fbpB) protein and not the 32A kDa Ag85A (fbpA) protein. The 30 kDa protein claimed in the instant application is Ag85B (*fbp*B, Rv1886c, see instant specification, paragraph [0075]). This assertion is supported by the co-inventor of the Orme patent, John T. Belisle in his 1997 publication (Science 276:1420-1422, 1997) a copy of which is attached hereto as Appendix B. On page 1421 first column of Belisle, Ag85 proteins A, B and C are the products of genes *fbp*A, *fbp*B and *fbp*C, respectively. Furthermore, the polyacrylamide gel of Figure 1 of Belisle depicts Ag85A, B and C, the bands of which are distinguishable from each other. Therefore, contrary to the statements in Orme, Orme does not disclose, and therefore does not enable, a prime-boost strategy using the 30 kDa major extracellular protein (Ag85B). Orme only enables boosting with the Ag85A (32A kDa major extracellular protein), the gene product of Rv3084c, or *fbp*A.

A claim is anticipated under 35 U.S.C. §102 only if each and every element as set forth in a claim is found, either expressly or inherently described, in a single prior art reference (MPEP §2131; *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d, 628, 631, 2 USPQ2d 1051 (Fed. Cir. 1987)). A claimed invention is anticipated only when it is "known to the art in the detail of the claim." *Karsten Manufacturing Corp. v. Cleveland Golf Co.*, 242 F.3d 1376, 1383 (Fed. Cir. 2001). In other words, not only must the limitations of the claim be shown in a single prior art reference, the limitations must be "arranged as in the claim." *Id.*

The Horwitz et al. and Belisle et al. publications are also submitted herewith in an Information Disclosure Statement.

Furthermore, Applicants disagree with the Office's statements on page 3 of the OA that "[furthermore, determination of a molecular weight is usually an approximation at best, what one of ordinary skill in the art may call a band 32 kDa, another looking at the exact same band on the exact same gel, may call the same band 30 kDa. In other words, Applicants have not shown that the M. tuberculosis major extracellular protein identified solely by a molecular eight of 30 kDa, excludes Ag85A." Well known, previously characterized proteins are often referred to only by their molecular weight, which is accepted in the art. The 30 kDa and 32 kDa Mycobacterial major extracellular proteins were well known in the art and had been characterized at the time of the invention of the subject matter of the instant claims. As demonstrated in the references attached in Appendices A and B, these proteins had previously been characterized and reference thereto solely by molecular weight would be understood by persons of ordinary skill in the art. "What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94.

Orme does not provide an enabling disclosure of a prime boost strategy using the 30 kDa major extracellular protein and therefore does not anticipate the claims of the instant application. Applicants respectfully request the withdrawal of the rejection of claims 27-32, 41-43 and 44-46 under 35 USC §102(e).

35 U.S.C. §103 Rejections

The rejection of claims 27-30, 32, and 41-46 under 35 USC §103(a) as being unpatentable over Horwitz et al. (US 6,471,967) in view of Orme et al. has been maintained. Applicants respectfully disagree.

To maintain a proper rejection under 35 U.S.C. §103, the Office must meet four conditions to establish a *prima facie* case of obviousness. First, the Office must show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the Office must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable

expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck,* 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the Office must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak,* 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Following *KSR Int'l Co. v. Teleflex, Inc*., this fourth prong of the *prima facie* obviousness analysis must not be applied in a rigid or formulaic way such that it becomes inconsistent with the more flexible approach of *Graham v. John Deere*, 383 U.S. 1, 17-18 (1966); 127 S. Ct. 1727 (2007). It must still be applied, however, as the TSM test captures the important insight that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* at 1741 (citing *United States v. Adams*, 383 U.S. 39, 50-52 (1966)).

The Office admits that Horwitz et al. do not teach of administering a second boosting immunogenic composition, which is a purified Mycobacteria major extracellular protein (OA, page 7).

As established *supra*, Orme does not provide an enabling disclosure for a prime-boost vaccine strategy with any protein other than Mtb Ag85A (the 32A kDa extracellular protein). Therefore, Applicants previous assertions regarding the "obvious to try" standard are valid.

In order to rely on the "obvious to try" standard under 35 U.S.C. §103, the Office must establish that there were a finite number of identified, predictable solutions with a reasonable expectation of success. *In re Fine*, 5 U.S.P.Q. 2d 1596, 1599 (Fed. Cir. 1988); *KSR Int'l Co. v. Teleflex.,* 127 S.Ct. 1727; *see also* Examination Guidelines, 72 Fed. Reg. at 57,529. Importantly, the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988).

As Orme himself demonstrates, not all combinations of vaccines produce protection against challenge with infectious pathogen (see Figure 8). Therefore, the

behaviors of the different boosting compositions are not predictable and the obvious to try standard cannot be applied. Since Applicant has established that Orme was not successful with the 30 kDa major extracellular protein, the prior art does not demonstrate success and there is not a finite number of identified predictable solutions.

For the reasons described above, the Office has not established a *prima facie* case of obviousness of pending claims 27-32, 41-43 and 44-46 over Horwitz in view of Orme. The cited prior art references, in combination, do not disclose all the claim limitations, and it is not "obvious to try" the claimed invention in light of the prior art references. The Office is respectfully requested to reconsider and withdraw the rejection of claims 27-32, 41-43 and 44-46 under 35 USC §103 based on Horwitz in view of Orme.

CONCLUSION

In light of the arguments presented *supra*, Applicants respectfully assert that the pending claims are in condition for allowance and request that a timely Notice of Allowance be issued in this case.

The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 50-3207.

Respectfully submitted,

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